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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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COHEN, PONTANI, LIEBERMAN & PAVANE LLP
551 FIFTH AVENUE
SUITE 1210
NEW YORK, NY 10176

EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
4161	

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10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,737	SEGULA ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-27 are currently pending. Claims 1-25 are withdrawn. Accordingly, claims 26-27 are the subject of this Office Action. This is the first Office Action on the merits of the claims.

Information Disclosure Statement

2. All references have been considered.

Priority

3. The earliest effective filing date afforded the instantly claimed invention has been determined to be 06/30/2004 as to claims 26-27.

4. Acknowledgment is made of Applicant's claim for foreign priority pursuant to 35 U.S.C. 119(a) and 365(b) based on prior applications filed in Germany on 07/22/2003 and 07/01/2003. The certified copies have been filed in parent Application No. PCT/EP04/07131, filed on 06/30/2004.

Election/Restrictions

Applicant's election of Group II, drawn to a method of making a sustained release pharmaceutical composition, in the reply filed on 08/25/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. The requirement is thus deemed proper and is therefore made FINAL.

Claim Objections

6. Claims 26 and 27 are objected to for depending from a non-elected claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. **Claims 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Lemmons et al* (WO 2003/039531) in view of *Kolter et al* (6,046,277).**

11. Instant claim 26 is drawn to a process for the manufacture of a sustained release pharmaceutical composition comprising Tamsulosin characterized in that the ratio between $Cmax_{fasting/fed}$ is equal to or less than 1.15, wherein the process comprises the steps of (i) providing Tamsulosin, optionally in combination with at least one excipient and (ii) applying a coating thereon which contains a combination of polyvinyl acetate and polyvinyl pyrrolidone.

12. Tamsulosin is known in the art. More particularly, *Lemmens et al* disclose "modified release tamsulosin tablets that exhibit little or no food effect" (Page 1, Lines 6-7). More specifically, *Lemmens et al* teach the pharmaceutical composition comprising a core of Tamsulosin (Page 11, Lines 1-6), a polymeric matrix such as "water swellable cellulosic derivatives... sodium alginate... acrylates... and polyvinyl pyrrolidones" (Page 11, Lines 10-12), and, optionally, excipients (Page 11, Line 21). Furthermore, *Lemmens et al* teach that "the tablets of the invention may be also protected by a suitable gastro-resistant coating" which includes "co-processed polyvinyl acetate phthalate (PVAP)" (Page 13, Lines 12-16). Additionally, *Lemmens et al* teach processes for manufacturing the invention which includes compression of tamsulosin into a tablet which is then coated with an enteric polymer (Pages 20-23, Example 3). However, *Lemmens et al* do not teach the process recited by instant claim 26 for the production of a composition comprising a core of tamsulosin which further contains a

coating having a combination of polyvinylacetate (PVAC) and polyvinylpyrrolidone (PVP).

13. *Kolter et al* teach the process of coating pharmaceuticals such as tablets with a coating containing PVAC and PVP. Specifically *Kolter et al* teach "the use of redispersible polymer powders or polymer granules consisting of polyvinyl acetate and N-vinylpyrrolidone-containing polymers for coating pharmaceutical or agrochemical use forms" (Column 1, Lines 6-9). More specifically, "Solid pharmaceutical use forms such as tablets, capsules, pellets, granules, crystals etc. are coated, i.e., provided with a film coating" (Column 1, Lines 12-13). And even more specifically, "This coating suspension is then sprayed onto pharmaceutical use forms by means of suitable equipment, e.g., horizontal drum coaters, coating pans, fluidized bed equipment, resulting in a uniform homogenous film which, after drying, requires no further heat treatment or curing" (Column 4, Lines 38-43). Accordingly, *Kolter et al* specifically teach the process of coating a pharmaceutical, such as a tablet, with a coating containing PVAC and PVP. Moreover, *Kolter et al* explicitly provide the motivation to coat tablets with a combination of PVAC and PVP, disclosing that "an unpleasant odor or taste can be masked, and swallowability can be improved. The stability of the active ingredient can be increased by the coating through less water and vapor and oxygen entering the interior of the tablet. The use forms have a better appearance and can be distinguished better by incorporating dyes. It is furthermore possible in particular to adjust the rate of release of the active ingredient by the film coating" (Column 1, Lines 15-22). Accordingly, for any and all of these reasons, a person of ordinary skill would have been motivated to

combine the teachings of *Lemmens et al* (which teaches the manufacture of a modified release tamsulosin tablet) with *Kolter et al* (which teach the manufacture of modified release tablets by coating tablets with a combination of PVAC and PVP) to result in the instantly claimed invention since it is advantageous to provide pharmaceuticals, such as tamsulosin, having increased stability and controlled release.

14. Claim 26 additionally contains the limitation (which is dependent from claims 25 and 22) that the Tamsulosin formed by the process of claim 26 is "characterized in that the ratio between maximum plasma concentrations of the Tamsulosin determined after administration of said pharmaceutical composition under fasting conditions and under fed conditions according to the $Cmax_{fasting/fed}$ is equal to or less than 1.35" (more specifically 1.15). However, the prior art does not specifically disclose the process of applying a coating which contains PVAC and PVP onto tamsulosin to provide a composition wherein the $Cmax_{fasting/fed}$ is equal to or less than 1.35, or more specifically 1.15. Nevertheless, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to carry out the process to provide a compostion wherein the $Cmax_{fasting/fed}$ is equal to or less than 1.35, or more specifically 1.15, for the following reason:

15. *Lemmons et al* teach that the $Cmax_{fasting/fed}$ of Tamsulosin is normally between 1.40 and 1.70 (Page 2, Lines 9-11). Furthemore, *Lemmons et al* teach that "It would be beneficial to make a tamsulosin pharmaceutical dosage form that exhibits reduced, little, or even no food affect. In this way, the dosage form would be safer; i.e. even if taken under fasted conditions, the risk of side effects is lessened" (Page 3, Lines 10-13).

Since Lemmons et al specifically provide the motivation to make a tamsulosin pharmaceutical dosage form that exhibits "no food effect" (which would encompass a $Cmax_{fasting/fed}$ of 1.00) the person of ordinary skill in the art would have found it obvious to use the teachings of Lemmons et al and Kolter et al - which teach process of applying a coating which contains PVAC and PVP onto tamsulosin as discussed above – to further provide a composition wherein the $Cmax_{fasting/fed}$ is equal to or less than 1.15.

16. **Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Lemmons et al* (WO 2003/039531) in view of *Kolter et al* (6,046,277) as applied to claim 26 above, in further view of NP Pharm, Sugar Spheres (Suglets®).**

17. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

18. As discussed above, the process of instant claim 26 is obvious under *Lemmons et al* in view of *Kolter et al*. However, neither *Lemmons et al* nor *Kolter et al* teach the process of providing a neutral core as recited by instant claim 27. As evidenced by NP Pharm, Sugar Spheres : Suglets® accessed online at http://www.nppharm.fr/suglets.htm and available online as of August 01, 2003 as demonstrated by the attached internet archive record , "Suglets are used as critical excipient for controlled or sustained release drug delivery technologies. Sugar spheres are inert pellets composed by sucrose and maize starch... are drug-free cores which are coated by a suspension or a solution of Active Ingredients... coating technologies are either a classic coating process or a fluid bed coating machine. The Suglets

sphericity allows a precise calculation of the drug quantity to spray on pellets. For a drug delivery system, a second polymeric layer is applied on pellets in order to obtain the desired dissolution profiles." Accordingly, NP Pharm teaches the use of a neutral (drug free and inert) pellet core which is then coated with active ingredient, followed by a second coating for controlled or sustained release drug delivery. Thus, it would have been *prima facie* obvious to a person of ordinary skill in the art to combine the teachings of *Lemmons et al* and *Kolter et al* - which teach the process of manufacturing a sustained release pharmaceutical composition comprising tamsulosin coated with a combination of PVAC and PVP as discussed above - with the teaching of NP Pharm to include in the process the step of providing neutral pellets which are then coated with the active ingredient (tamsulosin) followed by the coating containing a combination of PVAC and PVP, in order to achieve the desired and predictable results such as obtaining desired dissolution profiles.

19. **Claim-27 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Lemmons et al* (WO 2003/039531) in view of *Kolter et al* (6,046,277) as applied to claim 26 above, in further view of *Kato et al* (US 6,264,989).**

20. As discussed above, the process of instant claim 26 is obvious under *Lemmons et al* in view of *Kolter et al*. However, neither *Lemmons et al* nor *Kolter et al* teach the process of providing a neutral core as recited by instant claim 27. As evidenced by *Kato et al*, neutral cores are known in the art. Specifically, *Kato et al* teach that "Spherical particles used as raw materials of pharmaceuticals have been mainly used as seeds of sustained-release preparations and enteric coated preparations. Examples

of such spherical particles for pharmaceutical use include 'Sugar Spheres' made mainly of sucrose/corn starch, which is prescribed in the 'National Formulary (NF)'; and purified sucrose spheres..." (Column 1, Lines 22-27). Additionally, *Kato et al* teach spherical particles having "ideal properties as the cores for controlled-release pharmaceutical preparations" and provide "surface smoothness... leading to uniformity in the coating thickness of a medicinal agent layer or a release-controlling layer coated on the spherical particles. As a result, it becomes possible to control the thickness of a release-controlling layer which may influence on the release rates of the medicinal agent or to control the amount of the medicinal agent so as to be maintained at an effective blood level. Thus, sustained-release preparations can be designed optimally for intended application" (Column 18, Lines 25-37). Furthermore, the neutral core taught by *Kato et al* "advantageously provide increased granulation and coating efficiencies, leading to improved production efficiency and reduced cost" (Column 18, Lines 43-45). More specifically, Kato et al teach "the spherical particle itself can contain a medicinal agent. Therefore, for example, by applying a layer containing additional medicinal agent and a release-controlling layer on the medicinal agent and a release-controlling layer on the medicinal-agent containing spherical particle, a sustained-release preparation having three layers can be produced" (Column 18, Lines 46-51). Thus, it would have been *prima facie* obvious to a person of ordinary skill in the art to combine the teachings of *Lemmons et al* and *Kolter et al* - which teach the process of manufacturing a sustained release pharmaceutical composition comprising tamsulosin coated with a combination of PVAC and PVP as discussed above - with the teaching of

Kato et al to include in the process the step of providing neutral pellets which are then coated with the medicinal agent (tamsulosin) followed by a release-controlling layer (the coating containing a combination of PVAC and PVP), in order to achieve the desired and predictable benefits taught by *Kato et al*.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571)270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 4161

/Ashwin Mehta/
Primary Examiner, Technology Center 1600